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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/673,121 | 09/26/2003 | Shripad S. Bhagwat | 10624-133-999 | 1280 |

20583 7590 03/28/2006

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222 EAST 41ST ST
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| EXAMINER | |
|---|---|
| KIM, JENNIFER M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/673,121 | BHAGWAT ET AL. | |
| | Examiner | Art Unit | |
| | Jennifer Kim | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *2/9/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *78,80-82 and 88-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78,80-82 and 88-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 9, 2006 has been entered.

### Action Summary

1. The rejection of claims drawn to treating "cancer" or specified "cancer" drawn to claims 35-41, 47, 50, 55-61, 67-69, 75-78, 80-82 and 87 is hereby expressly withdrawn in view of Applicant's amendment.

Upon further consideration following rejections have been made:

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 78, 80-82 and 88-91are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 15-17 of copending Application No. 10/718,185. Although the conflicting claims are not identical, they are not patentably distinct from each other because it encompasses same subject matter. The difference between the copending Application and the instant claims is the mechanism of action "modulating of protein kinase" in copending Application for the same claimed effect (treatment of cancer). However, it would have been obvious that "modulation of protein kinase" is achieved upon administration of same compounds to same subject (cancer patient) to result in same effect. The mechanism of action set forth in the co-ending Application by which the active ingredient gives the pharmacological effect does not alter the fact that the same compound upon administration to treat a same subject suffering from cancer to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 78, 80-82 and 88-91 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "inhibition of JNK", does not reasonably provide enablement for the "treatment of cancer (i.e. colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine)." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

4. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors**

have been considered with regard to the instant claims, with the most relevant factors discussed below.

***Nature of the Invention***: All of the rejected claims are drawn to a method of treating cancer including colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine, responsive to JNK inhibition in a subject with an effective amounts of compound of structure set forth in claim 78. The nature of the invention is extremely complex in that it encompasses the actual treatment of a cell proliferation disorder (i.e. cancer of colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine) such that the subject treated with above compounds does not contract the specified cancer.

***Breath of the Claims:*** The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass treatment of cancer, a complex cell proliferation disorder responsive to JNK inhibition in humans which has potentially many different causes (i.e. many different mutations or combination of mutations). Each of which may or may not be addressed by the administration of the claimed compounds.

***Guidance of the Specification:*** The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually treatment of individual specified cancer is minimal. All of the guidance

provided by the specification is directed towards inhibition of JNK pathway in vitro rather than actual treatment of cancer in vivo.

***Working Examples:*** All of the working examples provided by the specification are directed toward the JNK inhibition in vitro rather than treatment of cancer in vivo.

***State of the Art:*** While the state of the art is relatively high with regard to treatment of cell proliferation disorder with specific active agent (i.e. breast cancer with tamoxifen), the state of the art with regard treatment of various cancer including colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine, with a single compound is underdeveloped. **To the extent that the Application is directed to a method of treating cancer cells in vivo, which is highly speculative, a greater amount of evidence is required to show its operability in humans. It is to be noted that no data has been presented to establish that Applicant's compounds would act in the manner claimed as they related to the treatment of cancer in general. The difficulty in treating various cancers including pancreatic, liver, colon and skin cancers is clearly known to the art as evidenced by the Carter et al. reference of record at pages 361-365. This illustrates that of approximately 35 drugs tested only 3 showed definite evidence of drug activity in the pancreas and only 4 in the colorectal and colon. Applicant's data has been reviewed but does not**

**establish a correlation between the in-vitro tests performed and the use of the Applicants active agents in vivo to treat various cancer including colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine as claimed.**

***Predictability of the Art:*** The lack of significant guidance from the specification or prior art with regard to the actual treatment of cancer in a human subject with the claimed compounds makes practicing the claimed invention unpredictable in terms of actual treatment of cancer.

***The amount of Experimentation Necessary:*** In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in the model system to determine whether or not the combination is effective for the treatment of **any cancer**. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard to treatment of cancer in vivo data with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant

guidance form the specification of prior art regarding actual treatment of cancer in vivo with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat cancer in a subject by administration of one of the claimed compounds.

Therefore, a method of treating cancer in general including colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine responsive to JNK inhibition in a subject administering compounds set forth in claim 78 is not considered to be enabled by the instant specification.

***Response to Arguments***

Applicants arguments filed February 9, 2006 have been fully considered but they are not persuasive. Applicants argue that the compounds within this class have anti-cancer activity and the support for the enablement of the treatment of "cancer" with the compounds of amended claims is found in the remaining disclosure of Force because numerous kinase inhibitors which are currently in clinical trials for "cancer" and even predicts that due to the early success with agents targeting kinases. This is not persuasive because to the extent that the claim is directed to a method of treating **cancer in general in vivo**, which is highly speculative, a greater amount of evidence is required to show its operability in humans. It is to be noted that no vivo data has been

presented to establish that applicant's compounds would act in the manner claimed (inhibition of JNK) as they related to the actual treatment of cancer in general. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. In the instant case, the specification, in particular, the working examples merely show that the specific compounds having the formula set forth in claim 78 were tested for having inhibiting activity of JNK pathway and having the JNK inhibiting effect in vitro. Given the fact that any **significant cancerous target cell variation** involving colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine, it would be reasonably expected to **alter its associated of target cells in vivo**. Further, Applicants' data has been reviewed but does not establish a reasonable expectation of success the use of the applicants **active agents will treat in-vivo** for various types of cancer having different cancerous target cells including colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary, or uterine. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
March 13, 2006